

medical aspect of the question is coming more into prominence than hitherto. The general condition of the patient is more important than the local. Chronic cervical discharge may clear up in many cases with local treatment, but the uterus is frequently the channel for the excretion of toxic products, the result of intestinal stasis or rheumatic affections. Teeth are a source of chronic infection. Dieting, exercise, baths, intestinal lavage, and artificial sunlight all help towards a cure. If there is stenosis of the cervical canal or retained uterine discharge, as in cases of chronic subinvolution with defective uterine contractions, local treatment, such as dilatation, curettage, and drainage, is valuable. Drainage can be carried out by stitching a self-retaining rubber catheter into the uterus for five or six days and injecting a drachm of glycerin with a serum syringe into the tube several times a day. This does not disturb the patient, and can be done by a nurse. Glycerin drainage relieves the pain and uterine spasm of acute sepsis, such as occurs in salpingitis or pyosalpinx. It is used as a preliminary measure to operation, but in many cases of pelvic peritonitis the symptoms subside with drainage, and operative intervention is unnecessary. It is useless operating upon adherent tubes and ovaries if the uterine canal is stenosed. A preliminary dilatation and drainage is necessary. If pus is present in the tubes, and removal or some conservative operation is adopted, drainage of the pelvis is best performed by placing a wick of gauze in the pouch of Douglas and bringing one end out through a vaginal incision. Amputation of the cervix for chronic sepsis may give good results if pregnancy does not occur subsequently, but rigidity from scar tissue may complicate labour. I have seen several cases where Caesarean

section was necessary for this condition. The operation is not a desirable one in the case of young women. Hysterectomy for chronic sepsis is beneficial when drainage has failed, but it is not so frequently employed now that general methods of treatment are available.

The restoration of reproductive function, and not its destruction, should be the aim of the practitioner. A radical pelvic operation should not be performed before treatment of septic teeth or intestinal stasis has been tried. Hysterectomy, if performed, should, when possible, be limited to the supravaginal operation. Pauhysterectomy causes contraction of the vaginal vault, with subsequent dyspareunia or difficult intercourse. Hysterectomy not only causes sterility, but gives rise in some cases to domestic unhappiness and infidelity, both on account of its physical and mental consequences. The after-histories of cases when followed up may make one question the advisability of radical operations, which may physically benefit the patient but cause unhappiness in her marital relationships. If the uterus is removed and the ovaries are left, the cervix acts to a certain extent as a channel of excretion.

Tuberculous affections of the pelvic organs should be treated on the same lines as surgical tuberculosis—fresh air and sunlight. The recurrence of menstruation may cause attacks of pain and keep up the activity of the disease. X rays are of value in suppressing menstruation and thus bringing about physiological rest. The dose can be graded to be temporary in its effects.

I have merely touched upon the fringe of the subject of pelvic sepsis. My opinions are perhaps controversial, but they are at least the result of my experience.

"ACTIVATED" (IRRADIATED) FLUORESCIN IN THE TREATMENT OF CANCER.

BY

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(With Special Plate.)

Two years ago (in 1927) we tentatively initiated a method of treatment on cases of inoperable cancer involving the use of a soluble salt of fluorescein, followed by the application of a comparatively small dosage of α rays or radium.

This method, and the results obtained therefrom, formed the subject of preliminary communications by one of us (S. M. C.) to a meeting of the local Branch of the British Medical Association at the Hampstead General Hospital on February 9th, 1928, and to the Chemio-Therapeutic Section of the International Cancer Conference¹ which met in London in July of that year. On the occasion of the London conference we also demonstrated at the Royal Northern Hospital several cases of previously inoperable cancer, which, subsequent to varying periods of treatment, then exhibited no evidences of the malignant disease from which they were suffering when treatment by means of activated fluorescein was commenced.

ACTIVATION OF FLUORESCIN.

Fluorescein ($C_{20}H_{12}O_5$), which may be regarded as the prototype of a long series of acid phthalein dye-stuffs, is formed by heating to a temperature of $190^\circ C$. a mixture of phthalic anhydride (1 part) and resorcinol (2 parts). By the introduction of halogen atoms into its molecule most of the fluorescein produced is transformed into dye-stuffs known by the generic term of "eosins." Of these the most important is eosin ($C_{20}H_6O_5Br_2K_2$), well known

by reason of its extensive use in histological investigations. This is the potassium salt of tetra-brom-fluorescein, which is usually marketed rather than the sodium salt, which does not crystallize so well. On the other hand, fluorescein, which is quite insoluble in water, but readily soluble in alkaline liquids, is produced as the sodium salt, under the trade name of uranin. In the course of our investigations we have also made use of the potassium salt, but found it necessary to have this specially prepared.

For some years past it has been known, as the outcome of researches by von Tappeiner and Raab, Noguchi, Salant and Bengis, Pereira, and others, that when lowly organisms such as paramoecia, or embryonic cells, including ova and spermatazoa, are exposed to the action of daylight in the presence of a dilute solution of eosin or fluorescein they are rapidly killed, whereas if protected from light, as when the containing vessel is placed in a dark cupboard, no such lethal effect is produced. Many other dyes, dye-stuffs, and acridine derivatives, in addition to haemato-porphyrin, a derivative of haemoglobin, all of which fluoresce in the presence of light, exhibit similar properties. This fact has been abundantly demonstrated in the case of eosin, most recently by Pereira.

Eosin, and the similar iodine compound erythrosin, have, however, from the clinical point of view, the disadvantage as compared with fluorescein, that, especially if injected intravenously, they are found to be definitely toxic to the animal body, whereas fluorescein appears to be completely non-toxic even if administered in comparatively enormous doses. Thus experiments carried out by W. S. C. Copeman and D. Levi have proved that continuous administration of 1 per cent. fluorescein to mice, over a period of several weeks, in place of water, has no obvious harmful effect; while tadpoles can live in a 1 per cent. solution of fluorescein, if protected from light, for a shorter period of time.

Dr. H. Colwell, radiologist to King's College Hospital, is at present engaged in an investigation on somewhat similar lines with the aid of a grant from the Medical Research Council, but his report has not yet become available.

Recently, in view of suggestions received from Professor Lindemann, F.R.S., of Oxford, we have carried out a series of tests, clinical and experimental, on the action of fluorescein salts of metals other than sodium with, and

without, subsequent irradiation. These salts have been produced and placed at our disposal by the Research Department of British Colloids, Ltd., and of Messrs. Boots, Ltd., Nottingham, to whom we desire to express our thanks for the help thus afforded us. Some preliminary tests on animals have also been made with the fluorescent sodium salt of dichloranthracene-disulphonic acid, for the reason that von Tappeiner has recorded the observation that this salt, when activated by means of ultra-violet light, was found to exhibit a lethal action on paramoecia far more intense in degree than that exhibited by fluorescein when similarly activated.

In view of the facts referred to above, and as the outcome of discussion with Professor W. E. Dixon, F.R.S., of Cambridge, it seemed desirable to investigate the possibility of obtaining beneficial results in the treatment of cancer by the use of sodium fluorescein or other fluorescent salts irradiated by means of wave-lengths of more penetrative power than those constituting the rays of ultra-violet light.

Von Tappeiner, in extension of his experimental work previously referred to, and regarding the masses of rapidly growing cells of malignant tissues as having at any rate some similarity to embryonic cells in their biological characteristics, attempted the treatment of certain rodent ulcers of the face by exposure to daylight, or to the rays of ultra-violet light, after previous painting of the exposed surface with eosin. But it is somewhat difficult to determine from his paper to what extent his work in this direction was ultimately successful.

Our own work with fluorescein has, for the most part, been concerned with more typical carcinomatous growths, activating with rays of greater penetrating power in relation to the body tissues than those previously employed by von Tappeiner. These rays, so far as we have been able to determine, are not, as in the case of the rays of visible light or of ultra-violet light, productive in conjunction with fluorescein of visible fluorescence, but nevertheless exhibit a potent lethal action on malignant cells even when these are situated at some distance beneath the surface of the skin. To this end, when irradiating with x rays we have used a mild dosage averaging 6 Holzknicht units (three-quarters of a pastille dose) screened through 4 mm. of aluminium, further details as to the actual technique being set out in a later section of this paper.

During the earlier stages of this work we endeavoured to control our observations by treating a few patients with exposures to the ultra-violet rays from a mercury vapour lamp, in each case also after preliminary painting of the skin or ulcerated surface with a solution of fluorescein varying in strength from 2 to 5 per cent. As regards these cases it may be stated at once that in no instance did we meet with any favourable response.

METHODS OF USING FLUORESCIN SOLUTION.

For the most part fluorescein has been used in the form of the soluble sodium salt, but, acting on the suggestion of Professor Lindemann, F.R.S., that trial should be made of a salt of higher molecular weight, we are also testing the relative merits of its potassium and strontium salts, of which the former appears to be slightly toxic to mice, but not to human beings, when administered in considerable quantity, while the latter would seem to be as completely non-toxic as is the sodium salt. But, as in the case of other strontium salts, it is not, apparently, absorbed from the alimentary canal. A number of other metallic salts of fluorescein have been prepared for us, but have not proved suitable, either by reason of their toxicity or insolubility.

In view of the experimental results obtained by Pereira, demonstrating the fact that the strength of the fluorescent solution has an important bearing on the effect produced on embryonic cells when subsequently exposed to light, we have, as stated above, made use on various occasions of solutions varying in strength up to 5 per cent., of which we have apparently found that a 2 to 2.5 per cent. solution of sodium fluorescein is to be preferred.

In the case of ulcerated or fungating surfaces, or when dealing with comparatively superficial growths, the solution is painted over the affected area, and, in addition, for some

distance over the apparently healthy skin surrounding the growth. The object of this is to ensure, so far as possible, that any outlying malignant cells shall be acted upon. No danger to healthy tissues is involved in this extension of the painted area, as these are not affected by the fluorescein when subsequently irradiated.

As a matter of routine the painting is usually carried out on two or more occasions prior to irradiation. In this connexion it is perhaps worthy of note that in no single instance in which sodium fluorescein has been used has any pain been caused by the painting, even when the painted surface is ulcerated, or by subsequent irradiation of the painted areas. In certain cases of more deep-seated growths the fluorescein has been given internally to the extent of 30 grains or more of the sodium salt an hour or two before exposure to x rays—a dose which, thus far, has never given rise to any unpleasant symptoms. Sodium fluorescein being extremely diffusible, we thought that it might suffice to give the drug by the mouth, thus obviating difficulties incidental to intravenous injections. The effect of oral administration of 30 to 60 grains, preferably by cachets, is that in the course of a half to three-quarters of an hour the patient's skin becomes of a uniformly pale yellow colour. Elimination, which occurs mainly by the kidneys is, however, rapid, and the normal colour is slowly regained in the next few days.

Experimental work on mice shows that the resulting coloration of the internal organs is fairly uniform, although somewhat more marked and persisting longer in the wall of the bladder than elsewhere; and that it is not taken up selectively by malignant cells. Consequently, with the dosage employed, it would seem that sufficient concentration of the fluorescein has not hitherto been obtained in these instances, which may account for the fact that results have not been generally satisfactory.

We have recently obtained evidence to the effect that more satisfactory results in the case of internal growths may be expected from the administration of fluorescein by the intravenous than by the oral method, due possibly to a more rapid and intense concentration of the drug at any particular point being thus obtainable.

With the object of simplifying the routine of treatment by the fluorescein method, so far as may be compatible with efficiency, the following scheme has been devised:

1. Paint with fluorescein solution, and/or administer internally.
2. Irradiate with an adequate dosage of x rays or radium.
3. Repeat 1 and 2, *three times*, at intervals of a week.
4. Allow *three weeks' rest*.
5. Then repeat the complete cycle, as often as may be considered desirable.

This scheme, however, will doubtless require modification in the light of further experience.

RADIOLOGICAL TECHNIQUE.

It is necessary to make some brief reference to the theory, at present admittedly in need of confirmation, on which the technique is based.

Numerous salts of fluorescein have now been prepared, varying in their atomic weights and also in their chemical and physical properties. For various reasons the whole of the series has not yet been tried, but the great characteristic of the group is the property that they possess of being able to be "excited" under the stimulus of ultra-violet rays to emit visible radiation. Our results would be explained if these salts, under the influence of x rays or radium, produced some secondary radiation which has a definite lethal effect on tumour cells. What its wave-length may be we have at present no means of determining, though experiments on this point could and should be made, should opportunity permit. It must be firmly emphasized that the salts themselves are completely inert physically until they are stimulated, or "activated" as we call it, by either of the above-mentioned agents. Up to the present we have been using the sodium salt almost entirely, although theoretically a salt of higher atomic weight, such as that of potassium or strontium, should yield better results. All these drugs seem to be entirely harmless, whether taken internally, used as an enema,

injected into the bladder, etc., or painted on the skin. It is interesting to note in connexion with work on the bladder that sodium fluorescein, apart from its effect on malignant cells, has proved to be a most effective aseptic agent after irradiation for rapidly clearing up cystitis. Mr. Clifford Morson was, we believe, the first to make this observation in connexion with the use of fluorescein. It may also be mentioned that it has no unpleasant after-effects when administered internally.

The two most important points in connexion with the radiological technique are: (1) In all cases in which the fluorescein has been used the solution has contained 3 per cent. of sodium bicarbonate. This is very important because it has recently been discovered that neutral solutions are completely inactive. (2) The secondary radiations from sodium fluorescein are apparently only produced when the salt is activated by x rays of a certain penetration. We have found the best result is obtained by those rays which will penetrate a filter of 4 mm. of aluminium. Harder rays are not so serviceable, and softer rays are useless. In this connexion certain radiologists have requested more detail as regards kilovoltage, milliamperage, type of transformer used, etc. To give a really accurate answer would entail longer research. It has been found sufficient for practical purposes, so far, to give such an exposure as will turn a three-quarter Sabouraud B pastille (placed on the skin), all the rays having passed through a 4 mm. filter. It does not apparently matter whether the process takes five or fifty minutes. Actually at the Royal Northern Hospital, where most of the work has been done, a mechanical 10 k.v.a. transformer is employed, using a spark-gap, between points, of just under seven inches, and a Philips Metalix water-cooled horizontal therapeutic tube. This gives a three-quarter B in about ten minutes. Elsewhere one of us (C. G.) uses a four-valve set with an entirely different kilovolt reading, and only three milliamps as compared with four, but with an ordinary water-cooled diagnostic tube. The results obtained seem to be the same, although the time taken in irradiation is somewhat longer. The spark-gap in each installation is about the same, but probably owing to the different type of transformer these readings do not allow any immediate comparison of the x-ray spectra to be made.

Now it is obvious that, if we can only use a fairly moderate penetrating ray for excitation, there is a limit as regards depth in the body at which we can get results, consequently most of our more striking cases, and those which incidentally can be the most easily verified, are superficial growths, such as breast carcinomata, sarcomata, malignant glands, bone tumours in thin parts, secondary nodules at the site of operation scars, etc. An interesting point in connexion with deciding whether a case is a suitable one for treatment or not is the histological structure of the tumour. Apparently the more cellular the tumour the better the results, and vice versa.

On the seventeenth day from the commencement of the treatment, in a good many cases the first indications of retrogression of the growth may be looked for. Occasionally this occurs as early as the fourteenth day, and sometimes is delayed as long as three weeks. Progress seems to vary very much; sometimes it is quick at first and slows down afterwards, sometimes the reverse. In any case, so far as we can tell, four to six months' continuous treatment on these lines is necessary before one can form a definite opinion as to the probable result. Care must be taken in treating large fungating tumours, because the mass breaks down very rapidly, and the absorption of toxic products into the system may produce serious and possibly fatal results. In these cases, therefore, we suggest that only a portion of the growth should be dealt with at one time, the rest being shielded off by covering with lead rubber.

CLINICAL DETAILS.

During the past two years a considerable number of cancer cases have been treated by the fluorescein method, more especially at the Royal Northern Hospital, where, as doubtless is the case at other hospitals, certain patients, usually at an advanced stage of the disease, eventually find their way to the radiological department. These, which have included cases of recurrence after surgical and

other methods of treatment, as well as cases which when first coming under observation are found to be suffering from malignant disease in so advanced a stage as ordinarily to justify the diagnosis of "inoperable cancer," have, in the majority of instances, and as a routine measure, been treated with fluorescein subsequently activated by means of x rays or radium.

Thanks to the kindness of Sir Lenthal Cheate and others, a limited number of cases have become available for treatment at King's College Hospital, the Hampstead General Hospital, and elsewhere, in addition to a few private patients, but unexpected difficulties have rendered the amount of clinical material available all too small. Thus, at an early stage of the investigation, we applied to the Departmental Committee on Cancer of the Ministry of Health (of which one of us is a member) inviting them to offer facilities for such cases of inoperable cancer in the various metropolitan infirmaries as were in a sufficiently good state of health to be conveyed to a central radiological department for the weekly treatment. This led to the wholly unexpected discovery that the number of patients suffering from cancer, especially from cancer of the breast, entering these infirmaries has fallen remarkably during recent years, few cases, therefore, being available.

The first case treated by means of irradiated fluorescein, at St. Mary (Islington) Infirmary, Highgate, was one of a huge fungating spheroidal-celled cancer of the breast (measuring 7 by 5 inches) in a male patient aged 49. It was decided, in the first instance, to paint half of the mass only with fluorescein (2 per cent. solution of the sodium salt), the axillary half of the tumour being selected for this purpose so as to avoid as far as possible chance of the fluorescein solution spreading beyond the central line. The whole of the tumour was then exposed to a three-quarter pastille dose of x rays through a 4 mm. aluminium screen. This sequence of painting and irradiation was administered three times in all, at intervals of a week, with the result that, at the end of the month, while the sternal side of the tumour showed practically no change, the axillary (treated) portion had shrunk considerably, and had become much flattened as compared with the remainder of the mass.

Subsequently the whole area was painted and irradiated at similar intervals of time, resulting in the gradual removal of the whole protuberant mass, which, when first seen, was overlapping the surrounding skin, and in the centre was elevated to the extent of about an inch above it. Regeneration of apparently healthy skin gradually took place from the circumference inwards, and enlarged glands in the axillae disappeared; but for some months shreds of slough continued to separate from the base of the growth, eventually exposing a small portion of the surface of one of the ribs. Before the exposed area could heal over, however, the patient unfortunately died of broncho-pneumonia following an attack of influenza during the outbreak of that disease which prevailed during the early months of 1929.

Permission for a post-mortem examination was, however, obtained, and the medical superintendent of the infirmary in which the patient had been under treatment reported that no evidence of secondary deposits in the lungs or other organs was found, neither could any enlarged glands be detected in the axilla.

Photographs of this, our earliest case, taken at monthly intervals before and after treatment with activated fluorescein, were reproduced in the November, 1928, number of the *Journal of State Medicine*. The series of photographs illustrating our present paper were taken by one of us (F. C.) under identical conditions as regards lighting and distance from the patient, and are therefore strictly comparable. They demonstrate the effect produced on a fungating and ulcerated carcinoma of the breast by treatment extending over the short period of three months.

SUMMARY OF RESULTS.

During the period of seventeen months from January, 1928, to June, 1929, 70 cases of malignant disease (for the most part stated to be "inoperable") have been treated by means of "activated" fluorescein in the radiological

department of the Royal Northern Hospital. The tabulated list of cases kindly supplied by the secretary of the hospital affords, on analysis, the following results:

Apparent recovery	8
Much improved	20
Too recent for statement	7
No change	8
Not improved	2
Discontinued treatment	12
Dead	7
Prophylactic	6
	70

As regards patients treated elsewhere, four successful cases have been reported to us from King's College Hospital; two cases of carcinoma of the breast in private practice have apparently recovered; and several instances have come to our knowledge in which recurrent nodules on or near operation scars have disappeared. In a letter recently received from Drs. Dight and Cutter of Sydney, Australia, the writers say, *inter alia*: "We have tried the method in a number of cases ... and, so far, our results are very encouraging." They give certain details as to a case of "obstructive neoplasm of the oesophagus," treated by means of intravenous injections of 10 c.cm. of a 1 per cent. solution of potassium fluorescein in normal saline before each irradiation given at intervals of fourteen days, with the result that "whereas before the treatment the patient had difficulty in swallowing fluids, she now can take semi-solids quite easily."

Recently a test was carried out on similar lines to those adopted in our first case, radium, however, being employed in place of α rays.

The patient was a man, aged 39, who had been operated on at varying intervals on five separate occasions for sarcoma of the thigh. Recurrence having taken place in the form of a fungating mass measuring about 4 by 3 inches and raised above the surface of the surrounding skin, it was decided to treat it with radium, the inner half of the growth being also painted and injected with 2.5 per cent. Na-fluorescein solution. Radium was used in the form of radon, a number of tubes containing which were inserted around the periphery of the growth. Some weeks later letters were received from Mr. Clifford Morson, the surgeon in charge, and from Dr. Muir, medical superintendent of Whipp's Cross Hospital, stating, in each instance, that the effect produced was definitely more marked on the portion of the tumour treated with radium + fluorescein.

To Mr. Stanford Cade of Westminster Hospital we are indebted for the following notes of two of his cases, which also afford evidence that the simultaneous use of fluorescein may considerably augment the action of radium.

Case 1.—Mrs. A. S., aged 55. Atrophic schirrosis of right breast; fourteen years' history. Ulceration and tumour. Treated by me with radium application, and daily painting with fluorescein while the radium was in position. Complete disappearance of the lesions, although the total quantity of radium was much smaller than what I use as a rule.

Case 2.—Mrs. T. B., aged 50. Carcinoma of breast, secondary deposits above clavicle and in axilla. Same treatment as in previous case. Complete disappearance of mammary tumour and axillary glands; marked diminution of supraclavicular glands. In this case, too, in my opinion, the fluorescein has accelerated the reactions to irradiation.

Dr. Mottram,² experimenting with the cells of rat sarcoma with which other rats were subsequently inoculated, has shown that dosages of radium and of fluorescein, each incapable alone of exerting any appreciable restraining effect on the growth of the cell substance inoculated, nevertheless, in conjunction, though apparently irrespective of which is first applied, exhibit such summated action as to prevent growth of tumours in the majority of the subsequently inoculated animals.

The fact that it is possible so greatly to augment the action of radium by the concurrent use of fluorescein is obviously of considerable interest, and likely to prove of practical importance where perhaps only a minimal amount of radium is available for purposes of treatment.

Finally we desire to direct attention to a few points which we have found to exert a definite influence on the extent of success likely to be attained by the use of "activated" fluorescein in the treatment of certain forms of cancer.

(a) Cases which respond most satisfactorily are those in which other methods of treatment have not previously been employed. If the patient has already been subjected to

courses of α rays or radium, this fact will probably militate against obtaining useful results with fluorescein.

(b) The more cellular and rapidly growing (that is, the more malignant) the growth, the more readily is it likely to respond to treatment.

(c) When fluorescein is given internally, in the course of treatment of cases of breast cancer, enlarged glands in the axilla have been found to disappear although not themselves directly activated.

(d) In the case of superficial secondary growths, such as recurrent nodules on or near the scar of an operation wound, excellent results have been obtained by the injection with a hypodermic needle of a few drops of fluorescein solution into the substance of the nodule prior to irradiation. Treated in this way, secondary nodules even of considerable size may disappear with unexpected rapidity.

(e) Cases previously regarded as inoperable, after a course of treatment with activated fluorescein have, in certain instances, been found, at a comparatively early stage, to have undergone such changes as to render them amenable to surgical intervention with satisfactory results.

REFERENCES.

- ¹ S. M. Copeman: Report of International Conference on Cancer, London, 1928, p. 255.
² J. C. Mottram: *British Medical Journal*, January 26th, 1929, p. 149.

LESIONS OF LATENT SYPHILIS.*

BY

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(With Special Plate.)

SINCE 1906 I have made an intensive study of the histologic lesions of latent syphilis in relationship to the presence in these lesions of the etiologic agent of syphilis, the *Spirochaeta pallida*. The results of this work have been published from time to time in various articles in American medical journals. This study began with the demonstration of spirochaetes in the myocardium and with the establishment of the histologic entity of syphilitic myocarditis. The first studies were made with the Levaditi method; because of the length of time required for it and because of the large number of negative results obtained by this method from cases showing identical histologic lesions as those seen in positive cases, my attention was drawn to the necessity of developing a better staining method than the Levaditi. With the aid of my assistant Dr. Starry, there was perfected the Warthin-Starry silver-agar method, which possessed great advantages over the Levaditi method, notably in the reduction of time required, from ten days to ten hours or less, in the use of the method on single sections mounted on cover-glasses, thereby permitting a control of the histologic lesions, and finally in the much greater percentage of positive spirochaete finding. Through the use of this staining method the greater part of my work on latent syphilis has been carried out, but the method, although in our opinion much superior to the Levaditi method in every way, is still far from being a perfect method, in that it does not give more than 60 to 75 per cent. of positive spirochaete demonstrations in cases showing identical tissue lesions. This has led us to continuous experimentation with staining methods, and recently in my laboratory we have developed a silver-starch modification of the Warthin-Starry method which promises a higher percentage of positive results than with the old method.

The material upon which this study has been carried out has been chiefly necropsy material coming into my laboratory from the University Hospital clinics. As this hospital is a State institution, its patients are drawn from all over the State of Michigan, largely from the small towns and rural districts. It represents chiefly the lower middle-class population. The present necropsy service examines about

* A paper read in opening a discussion in the Section of Venereal Diseases at the Annual Meeting of the British Medical Association, Manchester, 1929.

S. M. COPEMAN, F. COKE, AND C. GOULDESBOUGH: "ACTIVATED" (IRRADIATED) FLUORESCENIN IN THE TREATMENT OF CANCER.

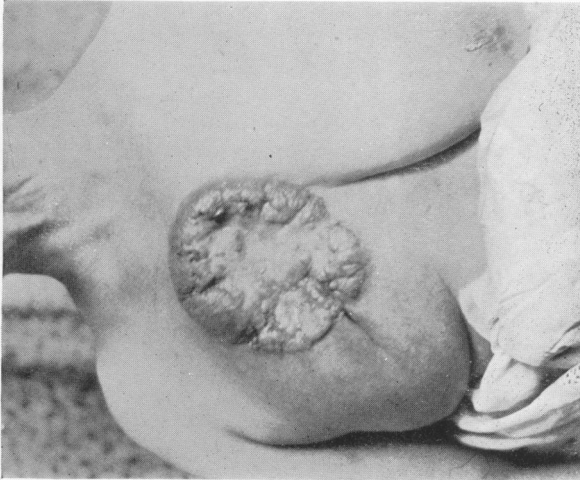


FIG. 1. October 1st, 1928.

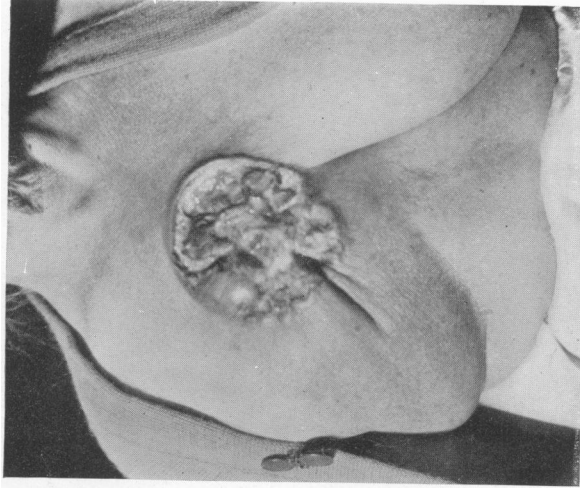


FIG. 2. October 22nd, 1928.

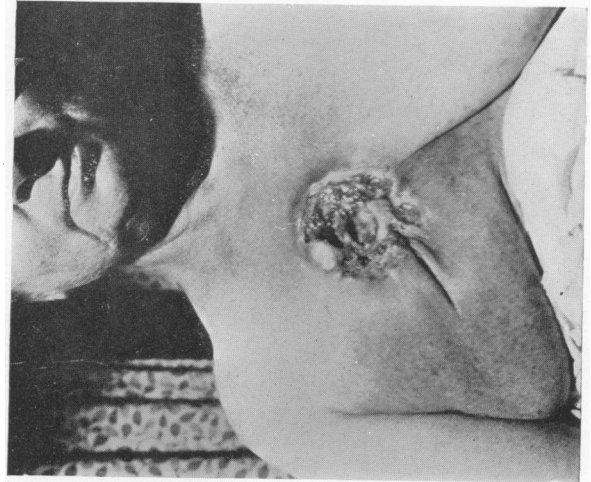


FIG. 3. November 5th, 1928.

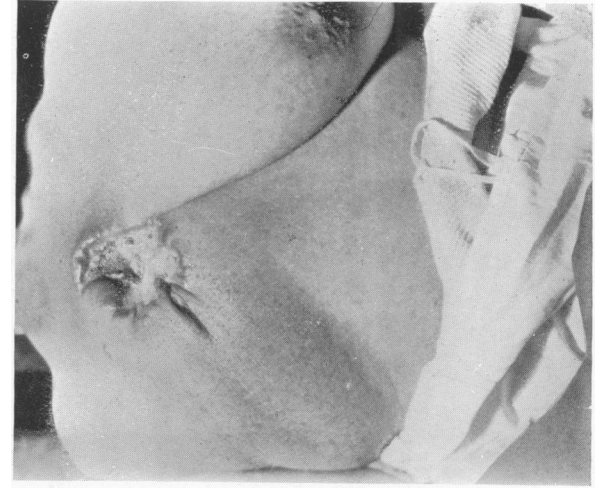


FIG. 4. December 31st, 1928.

D. E. BEDFORD AND H. JOULES:
BILATERAL SPONTANEOUS PNEUMOTHORAX.

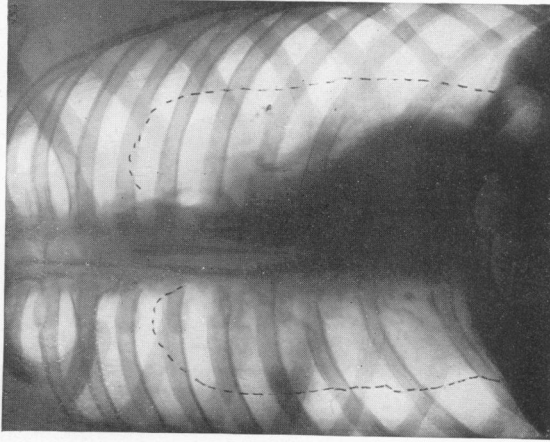


FIG. 1.—Radiogram taken on admission, showing bilateral pneumothorax. The limits of lung tissue have been outlined.

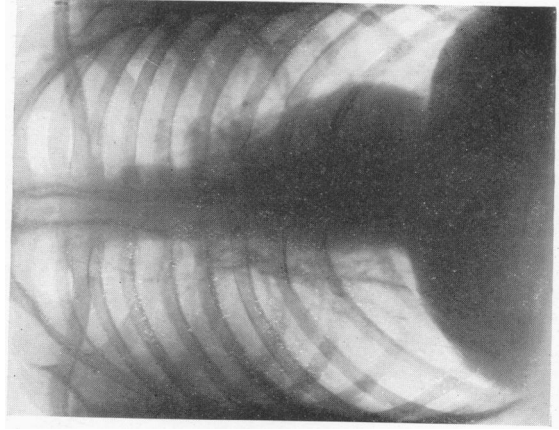


FIG. 2.—Radiogram taken on December 12th, 1928, showing complete re-expansion of both lungs and absence of any gross lesion therein.

AUG. 10, 1929]